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COMMUNICATION

Preliminary Evaluation of *Leucaena leucocephala* Seed Gum as a Tablet Binder

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ABSTRACT

The seed galactomannan of Leucaena leucocephala *Lam. de Wit var.K-8 (family Leguminosae), a natural polysaccharide, with properties comparable to guar gum, was evaluated as a pharmaceutical binder.*

Characterization was done using studies of compressibility, micromeritic, and mechanical properties of granules prepared by wet granulation and subsequent studies on compacts, both containing 5% w/w of binder. The seed gum was subsequently used as a binder with a badly compressible material, paracetamol, and studied likewise. The seed gum compared well with standard pharmaceutical binders (starch and polyvinyl pyrrolidone [PVP] K30), at least for properties studied herein.

INTRODUCTION

Leucaena leucocephala Lam. de Wit (family Leguminosae) is a medium to large tree (2–10 m tall), indigenous to Hawaii, but naturalized to India. The seed gum was found to contain up to 29% w/w of mucilage (1) which consists of galactomannan very much similar to that obtained from guar gum (*Cyamopsis tetragonolobus*, family Leguminosae). Soni et al. (2) have suggested *Leucaena* seed gum as a substitute for gum acacia in the food as well as pharmaceutical industry. Although abundantly available, the seeds of this tree are not reported to be utilized significantly and as such are of no current value. Particle size enlargement through granulation is a common particle design technique.

Binders are evaluated on different bases, such as mechanical properties of films (3), granules (4), and tablets (5), and compressional properties (6) of granules.

This study initiates an extensive focus on the understanding of the various properties of *L. leucocephala*

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seed gum and aims to arrive at clear conclusions after continued study. In the present study, the comparative evaluation of *L. leucocephala* seed gum as binder in tablet formulation was undertaken on the basis of micromeritic, mechanical, and compressional properties of granules. Lactose, a commonly used diluent with well-established consolidation mechanism (7,8), and paracetamol, a badly compressible material, were selected as materials for granulation.

MATERIALS

The fresh, authentic seeds of *L. leucocephala* var. K-8 were used for extraction of gum. Polyvinyl pyrrolidone (PVP-K30), starch IP, and lactose EP were also used. All solvents and chemicals used were of high purity grade. Other equipment used included: centrifuge (model R-24, Remi Industries, India); crushing strength apparatus (fabricated, Seema Enterprises, Pune, India); hydraulic press (Spectralab, Pune, India); Jasco V-530 spectrophotometer (Jasco Corp., Japan); Pfizer-type hardness tester (Cadmach, India); and Ro-Tap sieve shaker (Labtronics, Pune, India).

METHODS

Extraction of Seed Gum

Extraction was carried out as per the procedure described by Raval et al. (9), with a slight modification. The seed powder used for this extraction was of size 22 only. Use of hot water in the extraction procedure was substituted by demineralized water at room temperature, with multiple extractions. Seed gum thus obtained (henceforth called LLG-K8) was used for further study.

Preparation of Granules

Granules of lactose (200#) containing 5% w/w of binder (starch, PVP K-30, LLG-K8, gelatin, and guar gum) and those of paracetamol (85#) containing 8% w/w of binder PVP-K30, guar gum, and LLG-K8) were prepared using wet granulation method, air-dried overnight, and subjected to characterization of their micromeritic, mechanical, and compressional properties.

Characterization of Granules

Micromeritic Properties

The flowability of the granules (-16/+36) was assessed by determination of the angle of repose (θ) using fixed funnel method (10). The granules were subjected to bulk density determination.

Mechanical Properties

Crushing Strength of Granules

Crushing strength of granules (-16/+36) was determined using mercury load cell method as described by Jarosz and Parrott (4).

Friability of Granules

The friability of granules was determined by modification of the method of Ho and Hersey (11) in which 10 g granules was placed with 20 polyethylene balls (diameter 0.915 cm, weight 440 ± 5 m) in a ball mill and rotated for 5, 10, 20, and 30 min. Sieve analysis of the granules was carried out after each time interval. The friability index (FI) was determined using Rubinstein equation (12) as a function of time.

$$FI = [(d_g)_t/(d_g)_o] \times 100 \quad (1)$$

where $(d_g)_t$ = mean geometric diameter after time t, and $(d_g)_o$ = initial mean geometric diameter.

Compressional Properties

Heckel Plot

The compressibility behavior was studied using the Heckel Equation (13). Granules (500 ± 5 mg) were compressed on the hydraulic press (Spectralab) using a 13-mm flat-faced punch and die set, at pressures of 0.5, 1.0, 1.5, 2.0, and 2.5 tons for 10 sec. True density of the powder was determined by compression at 7.0 tons as described by Strickland et al. (14). The compacts were stored in an air-tight container for 24 hr to enable elastic recovery to occur; then the weight, diameter, and thickness were determined. The data were processed using Heckel equation and the mean yield pressure (P_y) was obtained.

$$\ln(1/1 - D) = kP + A \quad (2)$$

where k and A are constants and D is the packing fraction.

Tensile Strength

Hardness of the compact was determined using Pfizer-type hardness tester and the values were converted to tensile strength (T) by using following equation (15):

$$T = 2P/\pi Dt \quad (3)$$

where P = breaking force (kg), D = diameter (cm), and t = thickness of compact (cm).

RESULTS AND DISCUSSION

The modified method yielded 19.9–21.2% w/w of bright white *L. leucocephala* seed gum which turned to a stable off-white color on drying and storage. The *L. leucocephala* seed gum (1% solution) was subjected to various tests for absence of impurities and its purity was confirmed before being subjected to this study.

Micromeritic Properties

The seed gum of *L. leucocephala* yielded granules with flow properties markedly superior to other binders (Table 1). The results obtained with LLG-K8 are given in Table 1.

There was no significant difference in the angle of repose of LLG-K8 and those of starch or PVP-K30. Thus, LLG-K8, starch, PVP-K30 > gelatin > guar gum. The granules of paracetamol yielded identical results.

Mechanical Properties

Crushing Strength

The resistance of a granule to crushing is a necessary attribute of any granulation, which provides a uniform granule size irrespective of the extent and type of normal handling during processing. The resistance of the granule to crushing can be determined by various methods (4,16). The data obtained using Jarosz and Parrott load cell are shown in Table 2. The *t*-test for significance yielded results which are in fair agreement with the other data: guar gum > LLG-K8, gelatin > starch > PVP-K30.

Friability Studies

The friability index was calculated using the Rubinstein method along with analysis of change of friability index with time to determine surface and core strength of the granules. It was observed that friability index is a linear function of time, hence data were fitted with the equation

$$FI = -\beta_1 t + C \quad (4)$$

where β_1 and C are constants which reflect rate of production of fines and surface strength of the granule, respectively (Table 3).

Ho and Hersey (11) utilized the concept of production of fines as a function of time, but have not interpreted it quantitatively. Rubinstein and Ridgway (17) studied variation in the Brinell Hardness as a function of fraction of radius of the granule and demonstrated that the radial gradient in the binder concentration in the granule causes changes in the strength at different points across its radius, thus leading to differing surface and core strengths. This variation in the strength is highly influenced by properties of the binder.

Table 1

Micromeritic Properties

Placebo Granules			
Binder	Angle of Repose (°)	Bulk Density (g/cm³)	Viscosity (1% w/w) (cp)
PVP-K30	33.0433 ± 0.4529	0.4766 ± 0.0003	1.1546 ± 0.0284
Starch	36.3141 ± 1.5578	0.4552 ± 0.0002	1.6404 ± 0.0202
LLG-K8	34.3703 ± 0.6083	0.5174 ± 0.0021	5.4846 ± 0.0046
Guar gum	29.6769 ± 1.5289	0.4717 ± 0.0007	16.6384 ± 0.0031 (0.5% w/w)
Gelatin	29.6965 ± 0.7139	0.5205 ± 0.0008	
Paracetamol Granules (8% w/w binder)			
Binder	Angle of Repose (°)	Bulk Density (g/cm³)	
PVP-K30	32.8236 ± 1.9069	0.3847 ± 0.0008	
LLG-K8	32.0352 ± 1.2768	0.4743 ± 0.0008	
Guar gum	32.7587 ± 0.1208	0.3318 ± 0.0007	

Table 2

Comparative Data

Placebo Granules			
Binder	Crushing Strength (g)	Tensile Strength at $P_f = 0.8$ (kg/cm^2)	Mean Yield Pressure (P_y) (tons)
PVP-K30	420.821 ± 103.504	0.432	0.6622 ± 0.0626
Starch	460.809 ± 124.114	0.363	0.7113 ± 0.0906
LLG-K8	576.038 ± 61.758	0.250	0.7395 ± 0.0301
Guar gum	724.752 ± 117.458	0.165	1.6096 ± 0.0395
Gelatin	640.009 ± 261.016	0.535	1.7714 ± 0.1441
Paracetamol Granules (8% w/w binder)			
Binder	Crushing Strength (g)	Tensile Strength (kg/cm^2)	Mean Yield Pressure (P_y) (tons)
PVP-K30	425.124 ± 104.225	0.450	1.7679 ± 0.1026
LLG-K8	600.221 ± 86.996	0.240	1.8986 ± 0.1583
Guar gum	714.568 ± 75.664	0.180	1.2450 ± 0.0974

Starch shows high FI_5, which suddenly decreases and then follows linearity, which may be attributed to improper distribution of the binder in the granule (17). Gelatin and starch show very good surface strength. The higher C values for these two are indicative of uneven strength. Linearity in the latter stages indicates good core strength, and initial linearity indicates good surface strength. From the above discussion and Fig. 1 (with respect to surface strength), gelatin > LLG-K8 > starch > PVP-K30 > guar gum.

Compressibility

Heckel Plot

York and Pilpel (18), and Kurup and Pilpel (19) have suggested that Heckel equation is more sensitive as compared to the Cooper–Eaton equation in analysis of compressional behavior of soft material. The mean yield pressure (P_y) values for the granules containing different binders were determined from slope of Heckel plot [$\ln(1/1 - D)$ versus P].

Table 3

Comparative Friability Data (by Regression Analysis)

Placebo Granules				
Binder	β_1	C	r	Friability Index After 5 min (FI_5)
PVP-K30	0.645	62.643	−0.892	61.303
Starch	0.560	73.923	−0.991	92.500
LLG-K8	0.876	97.629	−0.995	81.444
Guar gum	0.962	38.292	−0.914	38.481
Gelatin	0.768	102.893	−0.900	96.463
Paracetamol Granules (8% w/w binder)				
PVP-K30	0.916	42.577	−0.995	38.229
LLG-K8	0.938	48.925	−0.978	46.667
Guar gum	1.032	44.906	−0.954	43.163

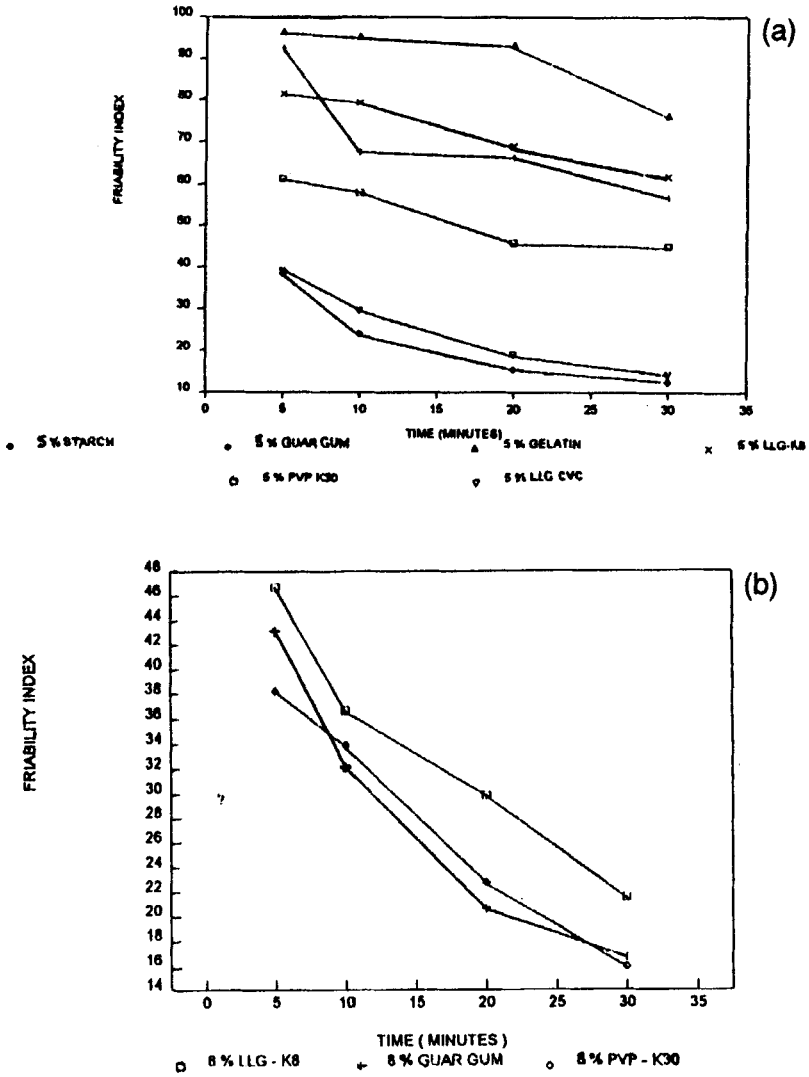

Figure 1. Plot of friability index versus time. (a) Placebo granules, (b) paracetamol granules.

For lactose, it is assumed that a table is made up of spherical isometric particles, and that fragmentation is the predominant mechanism of consolidation. Kurup and Pilpel (20) have studied compression characteristics of powder mixtures and have shown that starch and PVP can be considered as softer and more readily compressible materials. Starch undergoes plastic deformation (21) and PVP is considered to be elastic in nature (6). These materials, when used as a binder, will coat the powder particles and modify their surface characteristics. The effect of LLG-K8 coating on the compressional properties of the substrate was studied.

The packing fraction and the P_y value reflect the compressional characteristics of the material. The lesser the P_y value, the more is the tendency toward plastic deformation. It is reported (22) that 10% w/w lactose drastically lowers the toughness and the resilience of PVP-K30, and those of starch are only slightly modified. *Leucaena* seed gum was found to be comparable to starch and PVP-K30 as regards P_y. This suggests that the granules of all three binders consolidate at low pressures, giving good compacts. Guar gum and gelatin give hard granules. Thus, LLG-K8, PVP-K30, starch > guar gum > gelatin. Paracetamol granules show identical results.

Tensile Strength

The tensile strength of a compact is the measure of the strength of the compact produced; ideally, a high

tensile strength at low consolidation pressures would be best suited. PVP-K30 was the best compatible material, followed by starch. According to Reading and Spring (22), inclusion of lactose with PVP-K30 actually increased the bond strength of the film formed, and slightly lowered that of starch and gelatin. Thus, with respect to tensile strength of compacts, PVP > starch > LLG-K8. It is proposed that LLG-K8 may exhibit some elastic deformation as compared to starch and PVP, which is responsible for high granule strength but low tensile strength of compacts.

Paracetamol granules did not consolidate at low pressures. Increased concentration of guar gum improved the compactibility to values comparable to PVP-K30, but did not give good tensile strength, possible because of high elastic recovery and the formation of more binder–binder bonds rather than drug–binder bonds. Thus, for paracetamol:PVP-K30 > LLG-K8 > guar gum.

CONCLUSIONS

Placebo granules prepared using seed gum of *L. leucocephala* (var. K-8) as binder yielded large, uniform granules with good flow properties. The results indicate that this seed gum holds a lot of promise, and can be said to be comparable to standard pharmaceutical binders. Chemical modification of this polysaccharide as attempted by Raval et al. (23,24) may yield a semisynthetic analogue possibly with improved binder properties.

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